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ALAN J. CLARK

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THE DETECTION OF SUBCLINICAL LEAD POISONING IN CHILDREN OF PORTLAND, MAINE, SUMMER OF 1970

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INTRODUCTION

Lead poisoning is a major problem of all major cities of the United States. In New Haven, Connecticut, for example, between 1959 and 1968, out of 31 deaths in children due to accidental poisoning, 14 were attributed to lead.[23] Lead poisoning is such an insidious disease that active screening programs unveil subclinical as well as clinical cases of epidemic proportions. In Baltimore, Maryland known lead poisoning cases jumped from 56 in 1957 to 133 cases following two "lead-in-housing" surveys in 1958.[2] It was this kind of data coupled with the death of one of two known lead cases in Portland between 1967 and 1970 that prompted a search for subclinical cases of lead poisoning in Portland.

Most studies to date have been limited to large urban areas composed of mixed, principally non-white, ethnic groups.[7] This study was unique in that the population of Portland was 60,000 mostly made up of poor to middle income, English-speaking whites.

The method of screening a large group of children was based on a similar study completed in the summer of 1969 at Waterbury, Connecticut.[23] The urinary delta-aminolevulinic acid (ALA) test was chosen because one thousand tests could be performed within the budget and technical resources available in Maine at the time.

Also, since endemic lead poisoning was not known in Maine, there was no justification for subjecting one thousand children to venipuncture for the more expensive blood lead test, nor would the reception of the parent to such a program be as favorable.

The execution of this study was made with several assumptions: (1) It is generally agreed that stored lead is mobilized during the summer months.[3, 23] Acute toxicity, absorption of lead from the gut, and mortality due to lead are increased by heat and sunlight.[7] Thus a study performed in the summer months uncovers the greatest number of cases. (2) The metabolic toxicity of lead in the body is evident by an increase of delta-aminolevulinic acid in the blood, and consequently, in the urine. Lead inhibits many enzymes. One such enzyme, ALA dehydrase, joins two ALA molecules to form porphobilinogen, a precursor of heme.[12, 23] The decrease in the end product, heme, reduces the feedback inhibition of the ALA synthetase enzyme resulting in increased ALA production and ultimately urine excretion. Each individual tolerates different levels of lead without evidence of toxicity. Our environment is so contaminated with lead that it inevitably enters our food chain. There are few people who have no trace of lead in their body. This is also because lead may be readily inhaled from exhausts of gasoline engines.[25] (3) An ALA survey indicates the prevalence of lead

metabolic toxicity in the past in a population studied and not necessarily the presence of high blood lead levels.[23] (4) Elevated urinary ALA levels define a population to be evaluated further for treatment with chelation therapy, if blood lead levels are high.[5, 7, 14] If blood lead levels are not considered high enough to warrant treatment, closer supervision is indicated because the abnormal ALA test also reveals exposure and metabolic toxicity from lead in the past. (5) A blood lead level determination is a necessary next step to determine current lead poisoning, since only those children with high levels of blood lead will be treated with chelating agents.[1, 13] (6) The hematocrit does not correlate well with the blood lead level, but is helpful in determining both toxicity of the body burden of lead and interpretation of the blood lead level, since red blood cells carry most (90%) of the lead in the circulation.[3, 7, 10] (7) Eighty-five per cent occurs in one to six year olds. Therefore, this study concentrated on one to six year old children in pre-World War II housing in poor repair which presents the greatest source of lead poisoning.[2, 7] (8) Since parents of children most susceptible to lead poisoning are crisis oriented and thus unresponsive to preventive medicine, the screening test must be made extremely accessible to the parent.[7] New Haven in the past has experienced the lack of participation of the parent because of the insidious nature of sub-clinical lead

poisoning. Thus, we, as well as New Haven, instituted a door-to-door canvas technique with the aid of local youths for direct contact with the family.[15] This method gave the added advantage of personal contact for the education of anyone interested in learning about the problem.

The term, body burden of lead, will be used to discuss the level of total body lead toxic to an individual but which is not directly measured by any current method. Most of the lead is sequestered in bone and does not circulate in blood to the brain and other vital organs such as the kidney where it does the most damage until some as yet unknown factors stimulate its mobilization. Illness, ultraviolet light (especially common during summer months), and parathormone have all been proposed as responsible for mobilization of lead.

Blood lead tests may miss the fact that a child may have a high level of lead on board, because the lead is in a stored state and not necessarily mobilized to be detected as a high blood lead level. The danger of a blood lead determination is that a high body burden of lead may be missed by a spot test such as the blood lead test. The cost and testing time (at least twice those of the ALA test) plus the necessity for trained personnel to do venipunctures made the blood lead test less suited as an initial screening test for this study.

Other tests are available to study a "lead history" of the patient. Hair contains deposits of lead in one of the highest concentrations of any body tissue. If a hair is divided into segments, the segment closest to the root will reflect recent lead exposure while later segments give a history of lead exposure further in the past. This test is much more accurate in picking up recent and past but not acute lead exposures. The trouble is one test takes about a half hour and a run of ten takes one hour.[17] The funds and technical experience were not available to us for such a test.

The fluorocyte test for fluorescence of red blood cells under ultraviolet light in iron deficiency and lead poisoning only requires a finger stick. But the test was not suited because smears must be examined within twenty-four hours for accurate fluorocyte determination.[21,24]

The ALA test was at the time the least expensive and fastest to run (25-30 tests an hour) on a large population. It requires no technical skill to collect and may be obtained at the child's pleasure (which is a drawback in clinic collection, but not at home). Since the ALA test is extremely sensitive to even as low as .03mg% of blood lead and appears to remain elevated after the lead has disappeared from the blood either being sequestered in bone or excreted, the test was chosen as the best available for determining the incidence of

recent as well as past lead poisoning.[8] The ALA urine test is fraught with difficulty concerning the ready decomposition of the ALA molecule, the problem of urine concentration, and the uncertainty about the reported high incidence of false negatives, and the unknown time lag between lead ingestion and ALA increase. Considering all factors, the urinary ALA test should detect that segment of our population most fruitfully examined further by blood leads, since lead poisoning is currently defined by elevated blood leads. It is important to emphasize that no current test is accurate enough to diagnose lead poisoning and especially consistently detect a body burden of lead. The only sure way is to hospitalize a child and give him a trial dose of chelating agents, such as versene, and maasure the increase in lead excretion. But hospitalization is too impractical for screening purposes and chelating agents not without their own toxicity.

Five goals were set for the study: (1) the finding of current subclinical, but treatable, cases of otherwise unknown lead poisoning; (2) determining the incidence of lead poisoning in the population defined to establish the seriousness of the problem; (3) arrousing the local politic to support a continuing program of lead poisoning detection, treatment, and rehabilitation of the environmental sources of lead; (4) the educating of the professional and the non-professional in the severity, frequency,

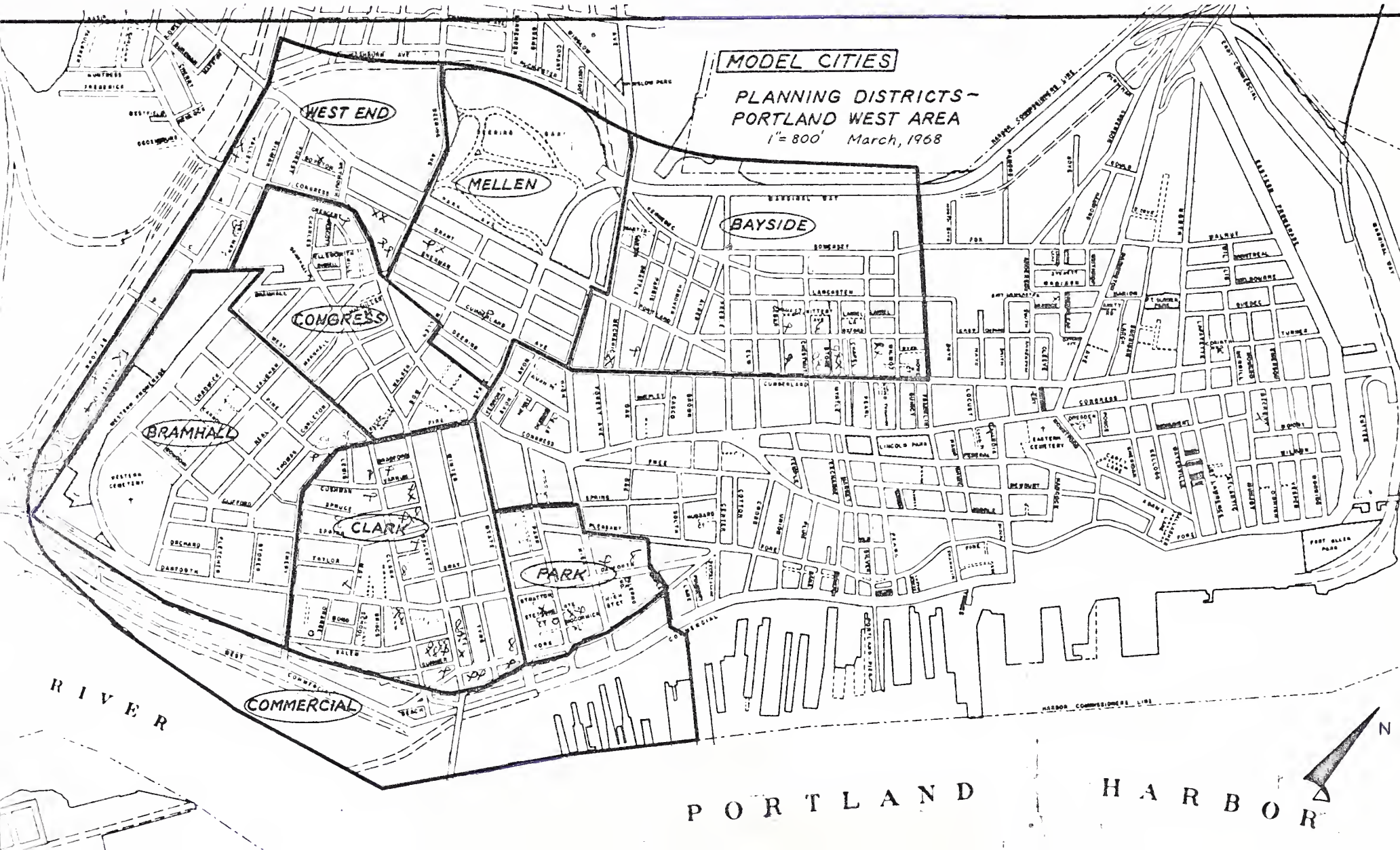
detection and prevention of lead poisoning and its sources; and (5) evaluating the screening program selected, the methods used, and comparing the results to those from other studies, in order to help develop a permanent program.

METHODS AND MATERIALS

The study was designed for the Model Cities Area of Portland, Maine. This study was funded by the Health Task Force of the Model Cities of Portland. It was supervised by Dr. George Hallett, Chief of the Department of Pediatrics, Maine Medical Center and directed by Alan J. Clark, Yale University School of Medicine, 1972. Dr. Charles Okey, Director of the State Department of Health and Welfare Laboritories, Augusta, Maine, administered the testing for the period July to September, 1970.

The Model Cities Area consists of the western section of the Portland peninsula, bounded by Route #1 to the west and north, Franklin Street to the east, and Portland Harbor to the south. The area is divided into seven residential districts; namely, Bayside, Bramhall, Clark, Congress, Mellen, Park and West End (Figure 1) . All except Bramhall contain pre-World War II housing in various states of disrepair. An estimated 1200 children, between one and six years of age by a 1968 census, live in these districts. The population is extremely mobile and census is inaccurate. Every door in all districts but Bramhall (because of its elderly population living in well kept stately homes) was visited at least twice at different times of the day until a contact was made. The aides

FIGURE 1
LEAD POISONING SURVEY, PORTLAND, MAINE, 1970



distributed leaflets to each door at least one day prior to the visit. They explained the problem under study and were often successfully persuasive. Six hundred and seventeen urine ALA tests were obtained from this population. Fifty-three more duplicate urinary ALA tests were obtained in the target area from the same children who also attended one of the seven day care centers or the Head Start Program visited. An additional two hundred thirty-five urinary samples of children who lived outside the Model Cities Area, but mostly in Portland or South Portland, were obtained.

The urine was collected in the middle of the day in 20 ml. glass bottles containing tartaric acid as a preservative to prevent decomposition of the ALA.[23] ALA is unstable. The bottles were immediately placed in "dark" metal containers and stored in a refrigerator before and after pick-up. Pick-up from the home was usually within twenty-four hours and from the centers within twelve hours. Shipment to the State Laboratory was by bus with a two-hour delivery time. At the most, each sample was exposed to only four hours without refrigeration, and never in direct sunlight. The ALA tests were performed within three to twenty-nine days following collection by the method of single chromatographic column handpacked with Dowex 50W-X8 resin. ALA was determined by a Beckman DB-G spectrophotometer at

553nm after ten minutes.[11]

Blood lead samples were drawn on all ALA tested children with more than 0.54 mg% and many siblings who themselves had normal ALA tests. The population of ALA normal children most likely to have high blood lead levels are siblings of ALA positive children. Thirty-three per cent of siblings of lead poisoned children are also affected.[2, 7] Therefore, if there are false negative ALA tests, the highest incidence should be detected by testing siblings.

Blood lead samples were taken from eighty-seven ALA trace and positive plus twenty ALA negative children in 10 ml. lead free vacutainers and tested by atomic absorption spectrophotometry (a.a.).[22] The a.a. method was significantly validated with a longer dithizone technique.[11] Heparinized capillary tubes were filled by finger stick for hematocrit determination. Blood samples were obtained by clinic appointment or home visit by the director.

Two weeks of television interviews, radio spots, several newspaper articles, leaflets and posters, were used prior to canvassing. Personal contact by the aides and director with leaflets during the eight weeks of sample collection completed the public education.

Preparation for the project was made in New Haven, Connecticut, with the help of the city public health

lead poisoning program and Yale Medical School resources with technical advice from the Connecticut State Department of Health and Welfare Laboratory in Hartford.

All statistical analysis was done using the conventions of Helen M. Walker and Joseph Lev in their book Statistical Inference, New York, 1953.

A chi-square (X^2) and analysis of variance (F) test were used to determine the significance (α) of values (X^2) and categories of values (F) from plain random distributions.

The z and student's test, t, were used for determination of the significance (α) of a difference between two values. Also used were the coefficients of regression (r_{xx}) and correlation (r) to determine the degree to which one type of data can predict values of another type. The significance (α) of an r correlation is determined by the probability of a hypothesis (H_o) that r is derived from a finite sample of a population with a true correlation of zero ($\rho = o$).

The confidence limits $C(x<P<y)$ are a range from x to y between which a proportion (p) obtained from a finite representative sample may exist for the total population (P) from which the representative sample came with a consistency of 95 or 99 per cent.

Any significance value (α) smaller than .02 was

considered by definition an indication of a non-random result. Any value with a 99% consistency or reproducibility has a significance of $\frac{100-99\%}{100}$ or .01 .

RESULTS

Nine hundred and five urinary ALA tests were performed of which fifty-three were duplicates. The distribution by district and age of the eight hundred fifty-two children are shown in Tables I and II respectively. In Table I there was a significant difference in frequency of positive and trace ALA urine results between Model Cities and Non-Model Cities children ($X^2 = 10.8, \alpha = .001$), but not between districts within Model Cities ($X^2 = 11.1, \alpha = .05$, if we disregard Bramhall area because of its small sample and accept only $\alpha \leq .02$). There was no difference in frequency of positive, trace, or negative ALA tests attributable to sex, (F=.52, 3.6, 0 respectively while $F_{.95} = 5.99$).

Analysis of results by age (Table II) reveals no difference in distribution of ALA results between ages one to six ($X^2 = 2.06$, $X^2_{.10} = 2.2$, $\alpha = .90$). Analysis of variance reveals that the ALA results are not derived from a random experimental procedure (F= 23.2, $\alpha = .01$, $F_{.99} = 6.93$). Nevertheless, there is a trend toward the highest incidence of positive ALA tests at two to five years, peaking at age three.

Table III shows results of one hundred twenty-one urine ALA tests from one hundred and seven individual and fourteen duplicates with one hundred and seven

associated blood lead levels. There is no significant correlation between the level of blood lead and the ALA level ($r=.199$, $H_0 : \rho = 0$, $r_{.975}=.195$, $\alpha=.025$), however, a positive trend is evident. The results only vary from random distribution by $\alpha=.25$, ($X^2=1.06$, $X^2_{.75}=1.3$). Two of thirty-two normal ALA tests corresponded to blood lead levels over .060 mg% giving a 6.2% rate of false negatives (or 15/32 (47%) false negatives with blood lead levels over .040 mg%), in the sample of nine hundred and five tests. This value is biassed on the high side because only a few normal ALA tests all from a high risk group of siblings of children with positive or trace ALA had follow up blood lead determinations. On the other hand, all positive and trace ALA tests were followed by blood lead tests. False positives were thirty-nine tests with blood leads less than .040 mg% out of eighty-nine positive ALA tests giving a rate of 44%. Note that values of blood lead between .040 and .059mg% can neither be considered normal nor seriously abnormal.

Table IV shows the levels of blood lead compared with the age of the children. In this case there was a significant relationship between age and level of lead in the blood ($X^2=22.96$, $X^2_{.999}=18.5$, $\alpha=.001$) (F for age=5.96, for blood lead=13.3, $F_{.99}=3.47$ and 3.70 respectively, $\alpha=.01$). The highest incidences of levels of lead over .060 mg% were at two, three, and four years

of age each being 26.7% of the total number of lead levels in the population over .060 mg%. Thus 85% of the children with high levels of blood lead were from one to four years old, while 93.5% were under six years old. The criterion of an abnormal ALA urine test gives a 55% incidence of blood lead over .040 mg% among children one to six years old.

Table V shows the correlations between hematocrit and urine ALA and blood lead ($r=-.128$ and $-.138$ respectively; neither r is significantly different from zero, Ho : $\rho=0$, $r_{.95}=.164$, $\alpha=.05$). Although the correlations were significantly small and not significantly different from $\rho=0$, the trend was negative in both. That is, hematocrits tended to be lower with high ALA or blood lead. Only one hundred and two hematocrits were drawn. Ten ALA duplicate results were also correlated with hematocrits.

Table VI demonstrates the length of time between the collection of the urine sample and the date of testing for ALA. The duration of storage of the urine sample from one to twenty-nine days did not alter, or especially decrease, the frequency of positive and trace positive ALA tests ($X^2=27.2$, $X^2_{.95}=28.9$, $\alpha=.05$).

Table VII shows the distribution of duplicate urine ALA tests. Fifty-three tests were duplicated. Nine were not consistent. The correlation of reliability

for the fifty-three duplicated tests is $r_{xx}=.212$, which is not different from zero (Ho: $\rho=0$, $r_{.95}=-.211$, $\alpha=.05$) . Fourty-four of fifty- three tests were consistent duplicates. The confidence limits are $C(.70<P<.93)=.95$.

Table VIII shows the proportion of children with pica for any non-food other than paint and pica with paint (i.e. paint chips or painted surfaces, toys, cribs). The incidence of children representing all treated cases with blood lead levels over .066 mg% and with a history of paint ingestion differed significantly from children with blood leads in the other two ranges ($<.045$ mg% and $\geq .045$ to $\leq .065$ mg%) ($z=4.05$, $2\alpha=.00006$; $z=2.38$, $2\alpha=.016$). Children with blood leads greater than .046 mg% but less than .065 mg% did not differ significantly from those with less than .045 mg% ($z=1.85$, $2\alpha=.07$). Pica itself without specific reference to paint or painted articles showed no significant difference in proportions reported in each category.

Table IX shows the proportion of cases living on the same street or in the same house along with corresponding confidence limits. The confidence limits represent these proportions obtained from a finite sample projected upon a larger more infinite population with a 95% accuracy. Twenty-four siblings had positive or trace positive ALA levels and twenty-two siblings had blood lead levels over

.040 mg%. The incidence of siblings affected by lead shown either in ALA or blood lead tests is not great enough to account for the total incidence of lead poisoning among children living on the same streets or in the same houses, except in the one category of the blood lead tests among children living in the same house. This shows that additional factors such as environment as well as family setting must be considered in lead poisoning.

Twenty-four of sixty-two (38.6%) siblings tested for ALA had trace or positive ALA with confidence limits $C(.28 < P < .53) = .95$. Twenty-two of twenty-nine (76%) siblings tested for blood lead had levels above .040 mg% with confidence limits $C(.65 < P < .85) = .95$.

The proportion of population with positive or trace positive ALA results is eighty-nine of eight hundred fifty-two or 10.4% with confidence limits of $C(.077 < P < .131) = .99$. The proportion of blood leads above .040 mg% for the population of eight hundred and fifty-two children can only be extrapolated from the sample selected with abnormal ALA and equals 48/852 or a minimum of 5.6% of the total population studied. The probable high rate of false negative ALA tests would indicate this value to be much higher.

TABLE I

LEAD POISONING BY MODEL CITIES DISTRICTS

ALA TEST

OF CHILDREN AGE ONE TO SIX IN PORTLAND, MAINE DURING

SUMMER, 1970.

URINE ALA RESULT	MODEL CITIES DISTRICTS BAYSIDE	BRAM-HALL	CLARK	CON-GRESS	MELLON	PARK	WEST-END	NON M.C.	TOTAL
NORMAL	128	5	245	24	47	30	57	227	763
TRACE	12	1	18	3	6	4	9	7	60
POSITIVE	8	0	15	0	2	1	2	1	29
TOTAL ALA TRACE - POSITIVE	20	1	33	3	8	5	11	8	89
TOTAL ALA TESTS	148	6	278	27	55	35	68	235	852
PER CENT INCIDENCE ALA TRACE-POSITIVE	13.5	16.7	11.8	11.1	14.6	14.3	16.2	3.4	10.4

ALA LEVEL

NORMAL - 0- 0.54 mg%

TRACE -0.55- 0.99 mg%

POSITIVE -1.00-10.00 mg%

TABLE II

URINARY ALA TEST LEVELS DISTRIBUTED BY AGE

IN YEARS OF CHILDREN OF PORTLAND, MAINE DURING SUMMER

1970

	AGE IN YEARS							
ALA RESULT	1	2	3	4	5	6	7+	TOTAL
NORMAL 0-0.54 mg%	35	91	126	151	203	115	42	763
TRACE 0.55-0.99mg%	4	3	14	12	20	6	1	60
POSITIVE 1.0-10.0 mg%	0	7	7	6	3	5	1	29
TOTAL ALA TRACE-POSITIVE	4	10	21	18	23	11	2	89
TOTAL ALA TESTS	39	101	147	169	223	126	44	852
PER CENT INCIDENCE ALA TRACE-POSITIVE	7.9	9.9	14.8	10.6	10.2	8.7	4.55	10.4

TABLE III

URINARY ALA LEVELS COMPARED TO BLOOD LEAD LEVELS OF CHILDREN AGE ONE TO SIX IN PORTLAND, MAINE DURING THE SUMMER, 1970

	BLOOD LEAD LEVELS in mg% *				
URINARY ALA in mg%	NORMAL 0-.039	BORDERLINE .040-.059	HIGH .060-.079	DANGEROUS ≥.080	TOTAL
POSITIVE 1.00-∞	8	15	5	1	29
TRACE 0.55-0.99	31	19	9	1	60
NORMAL 0-0.54	17	13	2		32
TOTAL	56	47	16	2	121+

*Only two children with positive ALA tests were unavailable for blood lead tests.

+Total includes 107 blood leads compared with 107 ALA and 14 duplicate ALA tests, or 121 correlations.

TABLE IV

BLOOD LEAD TEST LEVELS DISTRIBUTED BY AGE IN YEARS OF CHILDREN WITH TRACE OR POSITIVE ALA URINE TEST AT PORTLAND, MAINE DURING SUMMER 1970

BLOOD LEAD in mg%	AGE IN YEARS 1	2	3	4	5	6	7+	total
≤.039 NORMAL	(1)*	2(1)	10	8(3)	12(5)	6(1)	1	39(11)
.040-.059 BORDERLINE	2(1)	3(3)	7(1)	6(2)	10	4(1)	1	33(8)
.060-.079 HIGH	2	2(1)	4	4		1		13(1)
≥.080 DANGEROUS		2						2
TOTAL	4	9	21	18	22	11	2	87(20)+
≥.060	2	4	4	4	0	1	0	15

* Numbers in parenthesis are children with ALA negative and blood lead test taken.

\+ Although 89 children had trace or positive ALA, two were unavailable for blood lead tests.

TABLE V

HEMATOCRIT OF CHILDREN OF PORTLAND, MAINE DURING SUMMER, 1970 COMPARED TO BLOOD LEAD AND URINARY ALA LEVELS

	HEMATOCRIT (%)												
BLOOD LEAD in mg%	31	32	33	34	35	36	37	38	39	40	41	42	43
.016-.025	1		1					2	1	1			
.026-.035	1	1	3	1	2	7	4	3	2	3			1
.036-.045		2	3	7	4	4	3	2	4	2		1	2
.046-.055			3	2	3		2	1	2	3			
.056-.065				1	3	4		1	1			1	
.066-.075			2				1		1				
.076-.085					1	1							
.086-.105													
.106-.115	1												
TOTAL*	3	3	12	11	13	16	10	9	11	9	0	2	3
ALA in mg%													
0- .54	1	1	2	2	3	4	3	1	1	3		2	3
0.55-1.08	2	2	9	7	8	8	7	7	8	6		1	2
1.09-1.62			1	1	1	4	1	1	2	1			
1.63-2.16			1	1		1			1				
2.17-2.70													
2.71-3.24					1	1							
3.25-4.86													
4.87-5.40				1									
TOTAL*+	3	3	13	12	13	18	11	9	12	10	0	3	5

* Not all children with blood leads drawn had hematocrits determined. Total of 102 of possible 107 crits taken.

\+ Duplicate ALA tests are included. (102+10 duplicates=112)

TABLE VI

DELAY IN TESTING ALA URINE SAMPLES FROM DATE OF COLLECTION TO DATE OF TESTING AT PORTLAND, MAINE, SUMMER, 1970

DELAY IN DAYS	NUMBER AT URINARY ALA LEVEL			TOTAL NUMBER
	NORMAL	TRACE	POSITIVE	
1	8	1	1	10
3	83	1	1	85
4	55	2	2	59
5	20	2		22
6	65	2	3	70
7	56	3	3	62
8	50	6		56
9	42	2	3	47
10	98	8	8	114
11	37	4	3	44
12	56	10	4	70
13	63	5		68
14	32	1		33
15	57	6	1	64
16	36	4		40
17	3	1		4
18	1			1
19	6			6
20	19			19
21	9			9
22	7	1		8
23	3	2	1	6
24	3			3
26	3			3
27-9	2			2
TOTAL	814	61	30	905

ALA LEVELS

NORMAL -0 -.54 mg%

TRACE -.55-.99 mg%

POSITIVE-1.0-10.0mg%

TABLE VII

DUPLICATE ALA TESTS

ALA	NORMAL	TRACE	POSITIVE
NORMAL	42	3	1
TRACE	3	2	0
POSITIVE	2	0	0

TABLE VIII

PICA FOR NONFOOD OR PAINT AT VARIOUS BLOOD LEAD LEVELS

AMONG CHILDREN OF PORTLAND, MAINE, SUMMER, 1970

	BLOOD LEAD in mg%			CONFIDENCE LIMITS=.95	
INCIDENCE OF	<.045	.046-.065	>.066	.046-.065	>.066
	(1)	(2)	(3)		
PICA FOR ANY NONFOOD	50/71	20/28	7/7	C(.52<P<.86)	C(.65<P<1.0)
	(4)	(5)	(6)		
PICA WITH PAINT SPECIFIED	13/71	10/28	6/7		

Z VALUES OF DIFFERENCES BETWEEN COLUMNS IN EACH ROW OF TABLE VIII

	(2)	(3)	(4)	(6)	(2)+(3)	(5)+(6)
(1)	-.194 2α=.89	1.66 2α=.11			-.74 2α=.48	
(2)		1.61 2α=.11				
(4)				4.05* 2α=.00006		3.0* 2α=.005
(5)			1.85 2α=.07	2.38* 2α=.016		

* Significant difference obtained

TABLE IX

INCIDENCE OF LEAD POISONING BY STREET AND HOUSE

	POSITIVE OR TRACE ALA ($\geq$.55 mg%)	BLOOD LEAD ($\geq$.040 mg%)
	(1)	(2)
SAME STREET	60/89=.675 C(.55<P<.80)=.95	38/57=.666 C(.54<P<.76)=.95
	(3)	(4)
SAME HOUSE	38/89=.425 C(.31<P<.55)=.95	26/57=.456 C(.34<P<.56)=.95

Z VALUES OF DIFFERENCES BETWEEN VALUES IN TABLE IX AND PROPORTION OF SIBLINGS AFFECTED

SIBLINGS AFFECTED AMONG TOTAL POSITIVE TESTS ()	PERCENTAGE OF SIBLINGS AMONG POSITIVE TESTS COMPARED TO PERCENTAGE OF CHILDREN IN SAME HOUSE, ON SAME STREET			
	(1)	(2)	(3)	(4)
ALA TRACE-POSITIVE 24/62** =.386 (24/89) C(.28<P<.53)=.95	z=8.17* 2α=.00006		z=-2.95* 2α=.004
BLOOD LEAD $\geq$.040 mg% 22/29**=.76 (22/57) C(.65<P<.85)=.95		z=-5.5* 2α=.00006		z=-1.25 2α=.21

* Significant difference obtained.
** Total number of siblings tested

TABLE X

PER CENT OF POPULATION AFFECTED BY LEAD AS DETERMINED BY URINARY ALA OR BLOOD LEAD LEVELS IN CHILDREN OF PORTLAND

ALA POSITIVE-TRACE ($>$.55 mg%)	BLOOD LEAD ($\geq$.040 mg%)
89/852 = 10.4%	48/852 = 5.6%*
CONFIDENCE LIMITS	
C(.077<P<.131)=.99	C(.030<P<.070)=.99
α=.01	α=.01

*This is a minimum since this is determined from an ALA positive-trace population disregarding rate of false negative ALA tests.

DISCUSSION

The most important fact obtained by this study was that Portland, despite its relatively small size and uniform ethnic population, was not immune to the problem of significant levels of lead poisoning. At least 5.6% (disregarding a probable high omission rate due to false negative ALA tests) of the population of children one to seven years of age tested, had abnormal levels of blood lead over .040 mg%, and most of the children were between two and four years old. This figure is as high as that of four per cent experienced in Waterbury, Connecticut,[23] but not that of ten to twenty-five per cent quoted by Dr. J.J. Chisolm, Jr.[7] However, the incidence of abnormal ALA levels of 10.4% does match these figures of lead poisoning quoted by Dr. Chisolm.

ALA levels reflect toxicity of increased lead absorption at some time in the past. Blood leads reflect an equilibrium of lead in the blood with body stores. This equilibrium can be altered by many factors with unknown mechanisms. Blood lead values tend to be higher for a given population during the summer months reflecting the possible effects of heat, sunlight, and activity on the mobilization of bone tissue and lead stores of the bone.[3]

The reliability of blood lead and ALA determinations

should be suspect. Blood lead levels may reflect active mobilization of lead stores and acute ingestions, but not necessarily indicate the extent of body burden or chronic stable levels of body lead.[8] The ALA level may reflect toxicity of a chronic body burden of lead but not become detectable in cases of acute ingestion, and may remain abnormal after the body has rid itself of most of the lead through normal excretion.

The ALA test seems to be a method of establishing the incidence of abnormal exposures to lead in a population over an extended period prior to the study. It defines a population for further investigation and observation. It is an epidemiological tool and an ancillary test for determining lead metabolic intoxication. Blood lead levels should be used to monitor the state of mobility of the body stores of lead. At the time of mobilization, lead is most toxic as is evident by the increase in acute symptomatic plumbism during the summer when blood leads are the highest.[7] It is this fact which makes blood lead determinations a valid criterion for treatment. Yet it must be cautioned that a single low blood lead value does not represent a low body burden of lead.

From this study some important objective criteria for observing a child over an extended period for symptomatic lead poisoning can be gleaned: (1) The child two to four years of age from the pre-World War II housing

has a 10% chance of being lead intoxicated at some time, and at least a 5.6% chance of currently having a high blood lead. (2) Fifty-five percent of children with an abnormal urinary ALA test had a blood lead over .040 mg%. (3) Seventy-six per cent of siblings of a child with a currently high level of blood lead and thirty-nine per cent of siblings of a child with an abnormal urinary ALA test will be similarly affected. (4) In addition to the incidence of siblings affected, there is an added factor of the environment of the multiple family home and poor neighborhood which increases the probability that other children besides the proband are affected. (5) A child with a history of pica especially for paint has a 30% chance of lead intoxication.[2, 10] We find only pica with paint to be a significant concomitant with high blood lead values. It is important to stress that lead poisoning investigation should not wait for the signs of lead intoxication. The presence of these signs means that damage has already occurred. The signs of lead poisoning are protean, present in many other disorders, and need not be present with a high lead body burden. Their presence can only be used as confirmation of the diagnosis. Their absence <u>never negates</u> the presence of lead poisoning. Accidental ingestions, anemia, afebrile convulsions, lethargy, poor coordination, and slow development in one to five year

olds should be considered grounds for immediate lead poisoning investigation. (6) Any situation which separates mother from child, such as other children, a job, and emotional instability often predispose a young child to need fulfillment through excessive oral gratification or pica. The mother of a child with pica is often depressed, passive, and inactive. The family of these children is often crisis oriented, especially in health care.[5, 19, 20] All these factors commonly appear in the background of a child with pica and lead poisoning.

To date, six children in this study population have been treated with chelation therapy.[9] All six had blood leads above .060 mg% and abnormal urinary ALA. Four had lead lines in the long bones on x-ray. One had lead flakes in the abdomen. One was anemic at 31%. None had acute symptoms. One child came from a well-maintained home. The source of lead for this child was assumed to be dirt in which paint had dropped during the repainting of the exterior of the home during the spring. The other five came from poorly kept homes with rather unstable family situations. In these cases, interior paint seemed the likely source of lead.[9]

Serious questions about the urinary ALA test have been raised. Some objection to the test has been based on the method of disposable chromatographic columns.[4] The Connecticut State Laboratory has found the reliability

of the disposable columns very low , and has maintained a more reliable test with hand packed columns.

Another study has found that both blood ALA and lead determination have similar reliability, both with 8% false negatives. [10] Our data reveals 6.2% false negatives for urinary ALA with blood leads over .060 mg% (47% for blood leads over .040 mg%). Besides our biassed sample of false negatives, the different results could reflect the fact that the urinary ALA has an added factor of dilution and concentration due to kidney function. Although directions against urine sampling following oral intake of liquids were stipulated, there is no way to control for this factor where parents act as collectors. If the seriousness of false negatives is considered, only two normal ALA (6%) had a blood lead over .060 mg% and none over .080 mg%. This low percentage of false negative ALA results corresponded very closely with those in Dr. Joseph Davis' initial study with the urinary ALA test where 1.1% over .060 mg% and .14% over .080 mg% false negatives respectively were obtained. [14] It may be that most false negative ALA tests represent recent lead absorption where the lead is present in the blood but has not yet caused toxic effects as seen in ALA levels. There is no evidence as yet on the time involved between lead ingestion and increased ALA excretion.

The high rate of false positive and false negative

ALA results about an arbitrary value of .040 mg% for a high normal blood lead value may reflect that individual tolerance to metabolic toxic effects of lead varies at this level. Higher levels of blood lead are more uniformly toxic to all and thus yield a much lower, even acceptable, proportion of false negative ALA results. What can not be stated with certainty is whether the elevated ALA indicates, besides metabolic toxicity, a comparable toxicity to vital organs of that individual tested. Or does a false negative ALA indicate comparable vital organ tolerance? Chisolm advocates determination of both blood lead and ALA levels suggesting that a more serious lead poisoning state exists if both tests are elevated since blood leads indicate chelatable levels of lead and ALA indicates the deleterious effects of that level.[7, 8]

The fluorocyte test was not suitable for a field screening program because of the necessity to examine fresh blood smears because of rapid degradation of the fluorocyte phenomenon. With this in mind the stability of ALA needs discussion. Our study found no difference in rate of abnormal ALA tests stored up to twenty-nine days with tartaric acid preservative and in cold temperatures. Thus ALA did not decompose in storage. The possibility of the inadequate storage of samples by the parent before pickup still exists. In fact, several parents were known to have washed out the bottles con-

taining preservative contrary to directions.

False positives may be explained by similar arguments of concentrated urine and inconsistent collection techniques. But, most likely, false positives represent past exposure to lead. Obviously, the false positive ALA test is the least worrisome inconsistency.

Our study found a correlation between urinary ALA and blood lead of only .199 (significance α=.025). Davis found r=.91.[13] Coleman found a correlation of r=.51, α=.001 between blood ALA and blood lead.[10] Different criteria of population sampling and bias enter each result (i.e. Coleman used only clinic patients.). The most important conclusion is that the abnormal ALA test does reflect exposure to lead, and demands a further investigation.

Our experience with the ALA test confirms its usefulness as an economical initial screening test to establish the seriousness of lead poisoning in a previously unexamined area, provided it is not used as the sole determinant of lead poisoning. The serious question of false negative ALA results was not satisfactorily examined by this study. Extreme caution in the use of the urinary ALA test is warranted.

New techniques of dip-stick urinary ALA and finger-stick a.a. blood lead determinations may prove much better epidemiological tools for field surveys.

Despite all the controversy over the urinary ALA test it did find cases of unknown lead poisoning in a once (but no longer) complacent white community, and all for $3 a child!

It is important to note that among children screened by this method 55% had abnormal blood lead levels.

It is my hope that this study will stimulate others to seek out subclinical lead poisoning with whatever methods seem suited in other parts of the country not previously studied, especially beyond the provinces of university medical centers.

ADDENDUM

As a direct result of this study a strong "LEAD PAINT CODE" has been passed by the Portland City Government, a routine urine test for ALA is in effect in all well baby clinics in Portland. Both ALA and blood lead tests have been made available to all citizens in the State of Maine for the first time and free of charge. Efforts are underway in Augusta, Maine to coordinate lead poisoning programs throughout the state, And of course follow-up blood leads were taken on all children found initially with a level of .036 mg% or higher, while city public health officials made full investigations of all cases and helped educate the parent and correct the source of lead within the means of the city at the time.

SUMMARY

Eight hundred and fifty-two children, one to six, in Portland, Maine had urinary ALA tests during the summer of 1970. Eighty-seven (10%) of the children who had abnormal ALA tests and twenty siblings with normal ALA tests had blood lead determinations. Fifty-seven had blood leads over .040 mg%. Fifty-five percent of the children with abnormal ALA tests had an abnormal blood lead. Seventy-six percent of the siblings of a child with an abnormal blood lead were similarly affected. Six percent false negative ALA tests were found among children with blood leads over .060 mg%, but no false negative ALA had a corresponding blood lead level over .080 mg%. At least five percent (not considering a high omission rate due to false negative ALA tests) of the children, one to six years old, in Portland Model Cities Area had a blood lead over .040 mg%. The urinary ALA test with blood lead follow-up tests and careful clinical evaluation proved to be an economical and practical way to determine subclinical lead poisoning in a community not previously aware of the endemic problem.

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